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NOTES

Susceptibility of Anaerobic Bacteria from Several French Hospitals to Three Major Antibiotics

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The in vitro activity of cefoxitin was compared with those of metronidazole and clindamycin against 322 strains of anaerobic bacteria collected from several hospitals during 1982 and tested by an agar dilution method. Metronidazole and cefoxitin inhibited at least 89% of strains tested, whereas clindamycin was less active.

Continued updating of the susceptibility of recent clinical isolates and follow-up in changes of antibiotic patterns are periodically necessary in every country. When the same methodology is retained, an increase in resistance levels or local differences can be demonstrated (28, 29). Considering the lack of such studies in France, our purpose was to determine the antibiotic susceptibility of anaerobic bacteria, using the first data available by the reference method of Sutter et al. (25). For this reason, 322 strains isolated from human clinical samples were collected from 11 urban hospitals during the second half of 1982. MICs for the organisms tested were determined by the agar dilution method described by Sutter et al. (25). To assess the reliability of the method used, modal MICs of *Bacteroides fragilis* ATCC 25285, included in each batch of organisms, were calculated on the basis of eight measures for each antibiotic. Each measure was either equal to or within one twofold dilution of the mode in 96% of cases. The modes for clindamycin and cefoxitin were equal to or within one twofold dilution of those determined by Sutter et al. (25), who used the same methodology.

The susceptibility of the 322 strains to three antibiotics expressed as the range of MIC concentration of antimicrobial agent yielding inhibition of 50 and 90% of strains is shown in Table 1. All *Bacteroides ovatus*, *Bacteroides vulgatus*, *Bacteroides uniformis*, and *Bacteroides oralis* strains were susceptible to the three antibiotics. Metronidazole was the most effective agent against the *B. fragilis* group. All the strains tested were inhibited by 8 mg/liter, whereas 1 mg/liter was enough to inhibit 90% of *B. fragilis* isolates.

Cefoxitin at a higher dosage of 32 mg/liter inhibited all *Bacteroides thetaiotaomicron*, *Bacteroides distasonis*, *B. vulgatus*, and *B. uniformis* strains and 97% of the *B. fragilis* strains. A high level of clindamycin resistance (>128 mg/liter) was observed with 4 of 72 *B. fragilis* strains tested (5.5%).

The MICs for strains of *Fusobacterium* spp. were less than 0.125 mg of metronidazole per liter. *F. varium* was the only strain proving high resistant to cefoxitin (MIC >128 mg/liter). Metronidazole and cefoxitin remained active on most *Clostridium perfringens* strains; 97% of the strains tested were inhibited by 8 and 32 mg/liter, respectively. Some other strains had higher MICs but never exhibited high levels of resistance. Clindamycin was less active than the other two agents, and some strains showed higher MICs. All tested *Clostridum difficile* strains were susceptible to metronidazole and resistant to cefoxitin, and one strain was also resistant to clindamycin. Metronidazole at a dosage of 2 mg/liter inhibited 94% of *Clostridium* spp. other than *C. perfringens* and *C. difficile*, whereas cefoxitin at 16 mg/liter inhibited all of them, with the exception of two *C. ramosum* and one *Clostridium* sp. (MIC, 64 mg/liter).

Clindamycin demonstrated poor activity, as only 74% of the *Clostridium* spp. other than *C. perfringens* were inhibited by 8 mg/liter.

Considering all the gram-positive cocci and nonsporulated rods, cefoxitin at 16 mg/liter inhibited 93 of the 96 strains tested and appeared to be the most effective agent toward this group of bacteria. One isolate each of *Eubacterium rectale*, *Peptostreptococcus micros*, and *Streptococcus intermedius* required 64 mg/liter for inhibition.

Eubacterium sp. strains were susceptible to metronidazole and clindamycin, with some exceptions. Gram-positive nonsporulated rods other than *Eubacterium* sp. were mostly resistant to metronidazole. All *Peptostreptococcus* sp. were susceptible to metronidazole and clindamycin, and 10 to 15% of *Peptococcus* strains were resistant to these two antimicrobial agents.

Metronidazole is generally considered the most suitable agent for the treatment of infections due to the *B. fragilis* group, as few resistant strains have been described (3, 14, 16, 30). A high dosage regimen is needed for cefoxitin, as 48% of *B. fragilis* group strains tested had MICs equal to 16 or 32 mg/liter. Resistance to clindamycin is well known (1, 7, 16, 20, 21, 24, 27, 30), and our results corroborate those of Rolfe and Finegold (22) and Tally et al. (28). No difference among institutions can be statistically proven, as each hospital sent fewer than 10 strains of the *B. fragilis* group.

Most fusobacteria were susceptible to the antibiotics investigated here, but some strains (*F. varium* and *Fusobacterium* sp. strains) have been described as resistant to metronidazole (6), clindamycin (22, 23), and cefoxitin (2, 21). In view of the different susceptibility patterns of these organisms to various antimicrobial agents, a specification of the members of the *Fusobacterium* sp. group should be undertaken.

Good susceptibility of *C. perfringens* strains to metronidazole and cefoxitin has been observed, but some strains show

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TABLE 1. Comparative in vitro activity of metronidazole, clindamycin, and cefoxitin against anaerobic bacteria

Organism (no. of isolates)	Antibiotic	MIC (mg/liter)[a]			% Resistant[b]
		Range	50%	90%	
B. fragilis (72)	Metronidazole	0.125–8	0.5	1	0 (0)
	Cefoxitin	1–64	8	32	15 (3)
	Clindamycin	0.126–>128	0.25	8	14 (11)
B. thetaiotaomicron (13)	Metronidazole	0.125–2	0.5	2	0 (0)
	Cefoxitin	1–32	16	32	46 (0)
	Clindamycin	0.125–32	0.5	4	8 (8)
B. fragilis group (95)[c]	Metronidazole	0.125–8	0.5	1	0 (0)
	Cefoxitin	0.125–64	8	32	20 (2)
	Clindamycin	0.125–>128	0.5	8	12 (10)
C. perfringens (77)	Metronidazole	0.125–32	0.5	4	3 (3)
	Cefoxitin	0.25–64	1	8	5 (3)
	Clindamycin	0.125–64	1	16	17 (14)
Other clostridia (38)[d]	Metronidazole	0.125–32	0.125	1	5 (5)
	Cefoxitin	0.125–64	0.25	16	21 (16)
	Clindamycin	0.125–>32	1	16	29 (26)
Fusobacteria (14)[e]	Metronidazole	0.125–4	0.125	1	0 (0)
	Cefoxitin	0.125–>128	4	32	14 (7)
	Clindamycin	0.125–8	1	8	11 (0)
Eubacteria (20)[f]	Metronidazole	0.125–64	0.125	8	10 (5)
	Cefoxitin	0.25–64	1	8	10 (5)
	Clindamycin	0.125–>32	0.25	>32	20 (20)
Propionibacterium, Actinomyces, and *Bifidobacterium* spp. (13)[g]	Metronidazole	0.125–>128	128	>128	69 (69)
	Cefoxitin	0.125–1	0.25	0.5	0 (0)
	Clindamycin	0.125–>32	0.25	1	8 (8)
Peptococcus spp. (47)[h]	Metronidazole	0.125–>128	0.125	8	9 (9)
	Cefoxitin	0.125–8	0.25	1	0 (0)
	Clindamycin	0.125–>32	0.5	32	15 (15)
Peptostreptococcus and *Streptococcus* spp. (16)[i]	Metronidazole	0.125–0,5	0.5	>128	12 (12)
	Cefoxitin	0.125–64	0.5	64	12 (12)
	Clindamycin	0.125–4	0.125	16	15 (15)
All anaerobes (322)[j]	Metronidazole	0.125–>128	0.5	4	8 (6)
	Cefoxitin	0.125–>128	1	16	11 (4)
	Clindamycin	0.125–>128	0.5	16	16 (14)

[a] 50% and 90%, MIC required to inhibit 50 and 90% of the strains, respectively.

[b] Numbers are the percentages of resistant strains at the following breakpoints, based on data of Tally et al. (28): metronidazole, 8 mg/liter; cefoxitin, 16 mg/liter; clindamycin, 4 mg/liter. Numbers in parentheses are the percentages of resistant strains at higher breakpoints based on the criteria of Rolfe and Finegold (22): metronidazole, 16 mg/liter; cefoxitin, 32 mg/liter; clindamycin, 8 mg/liter.

[c] *B. fragilis* (72 strains), *B. thetaiotaomicron* (13 strains), *B. distasonis* (5 strains), *B. ovatus* (2 strains), *B. vulgatus* (1 strain), and *B. uniformis* (2 strains).

[d] *C. cochlearium* (2 strains), *C. clostridiiforme* (2 strains), *C. difficile* (3 strains), *C. tetanomorphum* (1 strain), *C. paraputrificum* (1 strain), *C. bifermentans* (3 strains), *C. butyricum* (1 strain), *C. septicum* (2 strains), *C. ramosum* (7 strains), *C. sporogenes* (9 strains), *Clostridium* sp. (4 strains), *C. rectale* (1 strain), and *C. celatum* (2 strains).

[e] *F. nucleatum* (5 strains), *F. varium* (3 strains), *F. mortiferum* (1 strain), *F necrophorum* (2 strains), and *Fusobacterium* sp.

[f] *E. alactolyticum* (7 strains), *E. rectale* (5 strains), *E. contortum* (1 strain), *E. lentum* (3 strains), *E. limosum* (1 strain), *E. ventriosum* (2 strains), and *E. combesi* (1 strain).

[g] *Actinomyces viscosus* (1 strain), *Corynebacterium matruchotii* (1 strain), *Bifidobacterium* sp. (2 strains), and *Propionibacterium acnes* (9 strains).

[h] *P. asaccharolyticus* (9 strains), *P. saccharolyticus* (4 strains), *P. prevotii* (6 strains), *P. niger* (1 strain), *Peptococcus* sp. (1 strain), *P. anaerobius* (22 strains), and *P. magnus* (4 strains).

[i] *P. anaerobius* (7 strains), *P. micros* (2 strains), *P. productus* (1 strain), *P. morbillorum* (1 strain), *S. intermedius* (4 strains), and *S. constellatus* (1 strain).

[j] Including *B. oralis* (2 strains).

higher MICs; 16 to 64 mg of metronidazole per liter (9, 10, 12) and 64 mg of cefoxitin per liter (21). Resistance to clindamycin has been previously observed (10, 18).

All *C. difficile* strains investigated were inhibited by 0.125 mg of metronidazole per liter. Resistance to metronidazole has only been demonstrated by Kesado et al. (20), whereas clindamycin resistance varies from 10 to 50% in previous reports (5, 20, 22).

Clostridia other than *C. perfringens* and *C. difficile* are inhibited by metronidazole, with some exceptions (1, 9, 10, 21). Cefoxitin at 64 mg/liter inhibited all strains in this study, which confirms the results of other reports (3, 8, 11, 17). Increasing clindamycin resistance of these clostridia has been previously demonstrated by Wilkins and Thiel (31) and Marrie et al. (21).

Resistance among *Eubacterium* sp. to metronidazole (3, 12, 14), cefoxitin (3, 4, 19), and clindamycin (4, 5, 8) has been shown. Metronidazole is generally ineffective on the other nonsporulated, gram-positive rods, contrasting with the good activity of cefoxitin and clindamycin; even some *Propionibacterium* spp. are resistant to the latter antibiotic, as suggested by Guin et al. (15).

Peptostreptococcus spp. were largely susceptible to the three antibiotics; only one, *P. micros*, was found with a higher MIC of cefoxitin (64 mg/liter), as reported by Drulak and Chow (11). Cefoxitin inhibited all the *Peptococcus* and

Streptococcus spp. whereas resistance is observed with metronidazole (3, 6, 21, 26, 30) and clindamycin (3–5, 19, 21, 26, 27, 30).

This study shows that clindamycin resistance occurred in several genera, such as the *B. fragilis* group and *Clostridium* and *Peptococcus* spp.

Metronidazole showed a very good activity against *Bacteroides* and *Clostridium* spp., whereas cefoxitin was more active against peptococacceae and nonsporulated, gram-positive rods.

If we had previously determined antibiotic susceptibilities by a broth dilution method (13), the change in methodology would prevent us from assessing any evolution, even though higher percentages of clindamycin resistance are observed. These results emphasize the usefulness of such studies in each country and the need for further investigations to demonstrate the change in susceptibility patterns.

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